

PEC UPDATE



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DoD PharmacoEconomic Center, 1750 Greeley Road, Building 4011, Rm. 217, Ft. Sam Houston, TX 78234-6190

DSN: 421-1271; Commercial: (210) 295-1271 Fax extension: 0323

WWW Homepage: <http://www.pec.ha.osd.mil> E-Mail: hscphaec@smtplink.medcom.amedd.army.mil

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Happy Valentine's Day



Comparison of Glipizide and Glipizide XL

The Department of Defense (DoD) PharmacoEconomic Center (PEC) has developed two models of cost effectiveness to help evaluate oral mono and combination therapy for the treatment of Type II Diabetes Mellitus (DM). During the development of the models, the PEC examined the properties of immediate release glipizide and sustained release glipizide (glipizide XL).

Information for analysis was obtained from healthcare providers at military medical treatment facilities (MTFs), peer reviewed medical literature, pharmaceutical manufacturers, the DoD prime vendor (PV) program and the Uniformed Services Prescription Database (USPD). As part of the PEC model development and validation process, the information was presented to a Tri-Service Surgeons General (SG) clinical consultant panel. The results of this process are summarized below.

Both the immediate and extended release formulations contain the

same chemical entity and therefore have exactly the same mechanism of action in regards to controlling blood sugar. Efficacy, indications for use, contraindications, warnings, precautions (drug interactions, pregnancy category C, use in nursing mothers, pediatric and geriatric use, carcinogenesis potential, impairment of fertility, and adverse reactions [side effects]) are the same for both formulations. The sustained release package insert claims a milligram per milligram equivalency between the two preparations.¹ The sustained release formulation ostensibly permits once daily (QD) dosing versus twice daily (BID) dosing for the immediate release preparation.

The diabetes clinical consultant panel was comprised of the U.S. Air Force SG Endocrinology Consultant, a senior U.S. Navy internal medicine physician (appointed to represent the Navy SG) and a senior U.S. Army family practice physician (appointed to represent the Army SG). All are practicing clinicians, actively

taking care of diabetics and participating in graduate medical education programs. The panel felt a mg per mg substitution was too much. They suggested half as much of the extended release formulation be used when switching between formulations (e.g., if a patient on 20 mg/day of immediate release was to be switched to the extended release formulation, the dose should be half, i.e., 10 mg/day). Patient compliance with QD versus BID dosing regimens was also addressed. Literature review reveals compliance of about 81% versus 78% with QD and BID dosing regimens, respectively.²⁻⁵ Reported compliance ranges in the studies overlapped for both QD and BID dosing regimens leading the panel to conclude that the literature demonstrates no significant difference in compliance between QD and BID oral dosing regimens. Additionally, the collective clinical experience of the panel indicated no clinically significant difference between the two formulations.

The panel felt that the extended release formulation often needed to be dosed BID versus QD and conversely, the immediate release could often be dosed QD. The USPD was queried regarding usage patterns for immediate and sustained release glipizide. Information was available from 33 facilities ranging from medical centers to small clinics for 13,331 unique patients. Of patients receiving glipizide, 43.7% of the prescription volume was for immediate release and 56.3% for sustained release. For the immediate release formulation, 57% of prescriptions were for multiple daily doses compared to 43% for single daily doses. In comparison, 20.3% of prescriptions for the sustained release formulation were for multiple daily doses and 79.7% for single daily doses.

While the USPD could not provide data on how well the patients were controlled, a significant number of sustained release prescriptions (one in five) were for multiple daily doses. A significant number of immediate release prescriptions (43%) were also written for daily doses. These data support the consultant panel observations. For fiscal year 1996, 58% and 17% of prescriptions for immediate and sustained release formulations, re-

spectively, were for multiple daily doses.

Current pricing [distribution and pricing agreements (DAPAs) as of 1 Dec 97 and 1 Jan 98] for immediate release 5 mg glipizide is \$0.018 to \$0.022 and 10 mg is \$0.032 to \$0.034 per tablet. A maximum dose of 40 mg per day costs \$0.128 to \$0.136 per day. The extended release formulation costs \$0.158 and \$0.315 for the 5 mg and 10 mg tablets, respectively. The maximum daily dose of 20 mg per day costs \$0.63, a difference of approximately five-fold. The slight potential improvement in compliance does not overcome the cost differential (4.5 to 5 times greater expense per day) of the sustained release (XL) formulation.

The clinical needs of many patients can be met with the immediate release formulation without a significant negative effect on compliance. The immediate release formulation provides a better value for DoD.

References:

1. Anonymous. Glipizide (Glucotrol XL) package insert, 1995.
2. Greenberg RN. Overview of patient compliance with medication dosing: a literature review. *Clin Ther* 1984;6:592-9.
3. Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette VL. How often is medication taken as prescribed? A novel assessment technique. *JAMA* 1989;261:3272-7.
4. Eisen SA, Miller DK, Woodward RS, Spitznagel E, Przybeck TR. The effect of prescribed daily dose frequency on patient medication compliance. *Arch Intern Med* 1990;150:1881-4.
5. Kruse W, Eggert-Kruse W, Rampmaier J, Runnebaum B, Weber E. Dosage frequency and drug-compliance behaviour - a comparative study on compliance with a medication to be taken twice or four times daily. *Eur J Clin Pharmacol* 1991;41:589-92.

Generic Acyclovir Available

The PEC recently evaluated oral antiviral therapies for the treatment of herpes zoster and genitalis. Agents commonly used in therapy include acyclovir, famciclovir, and valacyclovir. Clinically, all treatments are equally efficacious, safe and have the same side effect profiles. Compliance with all treatments is high regardless of dos-

ing regimen. Acyclovir has more indications for treatment and as of April 97 is available as an AB rated generic.

Analysis of FY 97 prime vendor data revealed 88% of purchases (\$3,776,951) for acyclovir were for the branded product. The same number of doses and strengths could be purchased as an AB rated generic for \$783,316 saving \$2,993,635. Purchasing an AB rated generic acyclovir can save MTF pharmacy dollars without loss of clinical efficacy.

In the Literature.....

Maximizing Cost-Effectiveness through Clinical Guidelines

Variation in both the cost and quality of health care has led to the development of numerous clinical guidelines, algorithms, and critical pathways. Through the use of guidelines, healthcare organizations or institutions can expect to maximize the efficient use of available resources.

In deciding on the best clinical option for an individual patient, decision makers must know both the expected costs and outcomes of competing treatment alternatives. The current climate of scarce healthcare resources dictates that options providing the greatest "value" should be selected first, and followed by those of less value if necessary. To date, the PharmacoEconomic Center has adhered to this philosophy in its pharmaco-economic analyses.

Choosing among competing treatment alternatives with different costs and effectiveness in a population with a wide variety of clinical conditions is a task of considerable complexity. A collection of mathematical techniques known as *optimization* (linear or nonlinear programming) is one method that has been used by industry to maximize or minimize a key variable such as cost or benefit (outcome). The airline industry, for example, uses optimization to efficiently

route a limited number of aircraft and flight crews to numerous cities across the country while minimizing cost.

Granata and Hillman¹, utilizing optimization, conducted a cost-effectiveness analysis by applying six existing clinical practice guidelines to a hypothetical cohort of 100,000 patients. The interventions consisted of prevention of hepatitis B, screening for colorectal cancer, diagnosis of stable angina, risk factor reduction in hypercholesterolemia and smoking, and treatment of recurrent ventricular arrhythmia. The purpose of the analysis was to compare and contrast the selection of clinical guidelines to maximize benefit for a population to the selection of the best guidelines available for treatment of individual patients while keeping costs within varying levels of constraint. Costs and effectiveness (life-years gained) from recent guidelines for the six interventions described above were entered into a computerized optimization model. The model was designed to analyze the cost and effectiveness of each intervention and select options based on the total cost-effectiveness for the population. The results showed that in 57% of available intervention opportunities, the guidelines providing maximal benefit for the population were different from those yielding maximal benefit for individual patients.

In conclusion, the authors point out that clinical guidelines designed to maximize cost-effectiveness for individual patients often fail to achieve maximal cost-effectiveness when applied to a population. Decision makers need to consider the clinical needs of their beneficiaries, available resources, and cost-effectiveness rankings of clinical alternatives for both individual patients and populations as a whole.

Reference:

1. Granata A, Hillman A. Competing practice guidelines: using cost-effectiveness analysis to make optimal decisions. *Ann Intern Med* 1998;128:56-63.

Upcoming Events

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Questions???

If you have further questions or comments related to DoD Pharmacy issues, please send them to the PEC *in writing* via fax (COM 210-295-0323; DSN 421-0323), e-mail (see address on front page) or the Feedback form on the WWW site (see address below). Please include your name, phone number, fax number, and e-mail address so we can respond to your inquiry.

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February

February 27-March 1

American Society of Health-System Pharmacists (ASHP) Future of Pharmacy in Managed Care Congress. Dallas, TX. Contact the ASHP at (301) 657-3000. www.ashp.org



March

March 1-5

American College of Healthcare Executives (ACHE) Annual Meeting. Chicago, IL. For information, contact ACHE at (312) 424-2800.

March 15-19

Combined Forces Pharmacy Conference. San Diego, CA. For information, contact LCDR Ted Briski at (619) 532-6170.